



## CONTINUING MEDICAL EDUCATION

# Questions and Answers

Ова рубрика (Q & A) садржи незнатно измењене сегменте из наведене литературе или за ову прилику написан текст. Циљ нам је да ови прилози послуже читаоцу као вежба за унапређење стручног енглеског језика.

[This section includes short segments of texts from the published literature or original texts. The main purpose is to provide questions and answers that readers can use to improve their English.]

*Scripta Medica*

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### Questions

1. What is the role of the cranial nerves in activities associated with vision and in the act of speaking?
2. What are the main characteristics of central retinal artery occlusion?
3. Describe the Purkinje Effect.
4. How did daltonism get its name?
5. The posterior portion of the eye is vascularized by three circulations (retinal, choroid, and optic nerve). How are each of these affected by hypertension?
6. Which are the key points for assessing ocular trauma?
7. How are specimens collected for microbiological analysis of eye infections?
8. Describe the etiology and diagnosis of left ventricular hypertrophy.
9. Define the term “genomics.”
10. Is there a significant genetic component affecting blood pressure and hypertension?
11. Arterial hypertension has a relatively low prevalence in children compared to adults. At what age should one begin to monitor blood pressure yearly in children?
12. A 16-year-old girl is brought to a physician by her mother, who states that her daughter has been steadily losing weight. The adolescent denies there is a problem and states that she is in no way underweight. The physician determines that the

girl is 5 ft 6 in tall and weights 90 lb. Which of the following laboratory tests is most helpful in assessing the severity of starvation in this patient?

- A. Complete blood count and differential white blood cell count
- B. Thyroid function studies
- C. Serum potassium level
- D. Determination of albumin in blood
- E. Liver function studies

13. The adolescent described above is diagnosed with anorexia. After stabilization of her nutritional status on a specialized inpatient unit, she is discharged home, with plans for follow-up therapy as an outpatient. Which of the following treatments have been shown to be effective in treating anorexia nervosa as an outpatient?

- A. Psychodynamic psychotherapy
- B. Family therapy
- C. Brief supportive therapy
- D. Group therapy
- E. Insight-oriented psychotherapy

14. A 46-year-old woman with stage III ovarian cancer presents to your outpatient clinic with nausea. The nausea has worsened over the past 2 days, and she is unable to consume anything beyond her medications and a few sips of water without vomiting. She is receiving chemotherapy with carboplatin and paclitaxel and notes that she has not had difficulty with nausea during or after chemotherapy because her oncologist administers antiemetics prophylactically before each session. It has been 17 days since her last chemotherapy. The nausea does not seem to occur with movement; it is worse after eating solids and liquids and is accompanied by abdominal distension. She has minimal abdominal pain, which is managed with oxycodone, 10 mg orally 3 times a day. Her last bowel movement was 4 days ago. Abdominal radiography (obstruction series) shows no air-fluid

### **Milka Mavija**

Department of Ophthalmology, University Medical Center Banja Luka, 78000 Banja Luka

### **Sanja Ilić**

Department of Endodontics, Institute of Dentistry, 78000 Banja Luka

### **Verica Pavlić**

Department of Periodontology, Institute of Dentistry, 78000 Banja Luka

### **Correspondence**

Verica Pavlić, DDS, Ph.D.

Department of Periodontology

Institute of Dentistry

78000 Banja Luka

levels, no free air, and no evidence of obstruction, but there is a moderate amount of stool in the colon.

Which one of the following is the most appropriate antiemetic to prescribe initially to this patient?

- A. Metoclopramide, 10 mg orally 4 times a day
- B. Ondansetron, 8 mg orally twice a day
- C. Promethazine, 25 mg orally (or suppository) every 6 hours
- D. Lorazepam, 1 mg orally every 6 hours
- E. Granisetron, 1 mg orally once daily

15. Name the hearing loss due to the aging processes.

16. Will a diet high in fructose, cholesterol, and saturated fats produce fibrosis of the liver?

17. What is the meaning of *editorial style*?

18. Water is ubiquitous in biology and in many other areas of nature. However, generally, water in tissues is not in the form of bulk liquid. Water in cells interacts with cell membranes, the surfaces of proteins, the interiors of proteins, and many other biological molecular species. Water plays a fundamental role in many diverse processes because it can undergo structural reorganization.

Are the dynamics of water very fast or slow?

19. Because reproduction is arguably the most important event in any animal's life, understanding how reproduction is regulated offers important insights into the evolution of a particular species. Learning how social and physiological factors collaborate to control reproductive activity is essential for understanding the selective pressures that shape reproductive control.

How does reception of social information reach brain regions responsible for initiating reproductive behaviors? How are gamete (sperm, oocyte) production and steroid hormone release controlled? Ultimately, how do social interactions influence gene expression to control reproduction?

20. What is the main dental concern for patients treated with the newer drugs for management of osteoporosis and malignant bone pathology?

21. Which serum biomarker may be used to indicate the risk of bisphosphonate-related osteonecrosis of the jaw?

22. What are the newest approaches in treatment of xerostomia?

23. Why do teeth change their color?

24. Which access has better outcome in ST-segment elevation acute coronary syndrome undergoing early invasive treatment: radial or femoral?

25. Can overweight as defined by body mass index (BMI) actually have a protective association with mortality?

### Answers

1. *Cranial nerve activities associated with vision.* Stimulation of the eye produces not only conscious visual sensations but also ancillary responses that utilize many peripheral nerves. The constriction of pupils to bright light and the focusing of the lens are effected via the parasympathetic fibers of the oculomotor nerve, whereas dilatation of the pupil in dim light is mediated via sympathetic fibers from the upper thoracic spinal cord levels. Pain from irritation of the cornea is transmitted by the trigeminal nerve. Blinking of the eyelid results from stimulation by the facial nerve; movements of the eye and raising the eyelid follow stimulation by the oculomotor, trochlear, and abducens nerves; the secretion of tears from the lacrimal gland results from stimulation of parasympathetic fibers of the facial nerve.

*Act of speaking.* Contraction and relaxation of the thoracic and abdominal musculature during exhalation and inhalation, mediated by spinal nerves, are essential preliminaries to the act of speaking. Vowels are formed by the vibration of the vocal cords of the larynx, which are innervated by the vagus nerve; resonance is aided by relaxation of the pharynx and palatine arch muscles (this is especially pronounced in singers), which are innervated by the glossopharyngeal and vagal nerves. Certain consonants, such as Ts and Ds, are formed by the action of the tongue, which is innervated by the hypoglossal nerve; others, such as Ss and Cs, are formed by the combined action of the jaw, tongue, and lips, involving the trigeminal, hypoglossal, and facial nerves. The lips alone form the consonant P through activation of the facial nerve.

2. *Sudden, severe, and painless loss of vision in one eye is characteristic of central retinal artery occlusion (CRAO).* The retina becomes opaque and edematous, particularly in the posterior pole where the nerve fibers and ganglion cell layers are thickest. The orange reflex from the intact choroidal vasculature beneath the foveola stands out in contrast to the surrounding opaque neural retina, producing the characteristic cherry-red spot.

The central retinal artery reopens or re-canalizes with time, and the retinal edema clears. However, the retinal arterial infarction generally has a devastating effect on visual acuity. In one study, 66% of CRAO eyes studied had final vision worse than 20/400, and 18% had vision of 20/40 or better. Most cases of 20/40 or better vision had a patent cilioretinal artery, which preserves the central macula. Loss of vision to the level of no light perception at all is often associated with choroidal vascular insufficiency (ophthalmic artery occlusion) in addition to occlusion of the central retinal artery.

3. *Purkinje Effect.* The Purkinje effect (sometimes called the Purkinje shift, or dark 2. adaptation) was named after the Czech anatomist, Jan Evangelista Purkyně, who noted that

light blue flowers appear bluer at dawn or twilight than at midday. At dusk, red flowers appear black.

The effect occurs because color-sensitive cones in the retina are the most sensitive to yellow light, whereas the rods, which are more light sensitive (and thus more important in low light) respond best to green-blue light, even though they do not distinguish colors. This is why humans become virtually color-blind under low levels of illumination, for instance in moonlight.

The insensitivity of rods to long-wavelength light enables us to use red lights under certain circumstances, as in the control rooms of submarines, in research laboratories, or during naked-eye astronomy. Submarines are dimly lit to preserve the night vision of the crewmembers working there, but the control room must be sufficiently lit for reading of instrument panels. Under red light, or with red goggles, the retinal cones receive enough light to provide photopic vision (namely the high-acuity vision required for reading). Because the rods are not saturated by bright light and are insensitive to long-wavelength red light, the individual can remain dark adapted, in case he needs to use the periscope at night, for example.

Red lights are also often used in research settings. Many research animals, such as rats and mice, have limited photopic vision, because they have far fewer cone photoreceptors. Red lights keep the animals “in the dark” (the active period for nocturnal animals), while allowing the human researchers, who have one kind of cone that is sensitive to long wavelengths, to read instruments or perform procedures that would be impractical even with fully dark adapted (but low acuity) scotopic vision. For the same reason, zoo displays of nocturnal animals often are illuminated with red light.

The Purkyně effect was discovered in 1819 by Jan Evangelista Purkyně, a polymath (knowledgeable man) who would often meditate at dawn during long walks in the blossoming Bohemian fields. Purkinje noticed that his favorite flowers appeared bright red on a sunny afternoon, while at dawn they looked very dark. He reasoned that the eye has not one but two systems adapted to see colors: one for bright overall light intensity and the other for dusk and dawn.

Purkinje wrote in his *Neue Beiträge* (translated from the German):

Objectively, the degree of illumination has a great influence on the intensity of color quality. In order to prove this most vividly, take some colors before daybreak, when it begins slowly to get lighter. Initially one sees only black and grey. Particularly the brightest colors, red and green, appear darkest. Yellow cannot be distinguished from a rosy red. Blue became noticeable to me first. Nuances of red, which otherwise burn brightest in daylight, namely carmine, cinnabar and orange, show themselves as darkest for quite a while, in contrast

to their average brightness. Green appears more bluish to me, and its yellow tint develops with increasing daylight only.

4. An article entitled “Deficiency of color vision” was published in 1798 by the English chemist, John Dalton. He described his own color blindness. Because of Dalton’s work, the general condition has been called *daltonism*, although this term in English now applies more narrowly to deuteranopia alone.

Colorblindness, or color deficiency, is a sex-linked characteristic found to some degree in 8 % of males and 1.5 % of females. There is no actual blindness but a deficiency of color vision. The most usual cause is a fault in the development of one or more sets of retinal cones that react to various wavelengths in light and transmit that information to the optic nerve. This type of color blindness is usually a sex-linked condition. The genes that produce photo-pigments are carried on the X chromosome. If some of these genes are missing or damaged, color blindness will be expressed in males with a higher probability than in females because males lack a second X chromosome. A functional gene on only one of the two X chromosomes in the female supplies the needed photo-pigments. Color blindness can also result from physical or chemical damage to the eye, the optic nerve, or parts of the brain. For example, people with achromatopsia suffer from a completely different disorder, but are nevertheless unable to see colors.

All classifications of colorblindness are based on subjective defects in perception, even though the specific cause is unknown. Individuals with three-color vision (trichromats) are those with 1) normal vision, 2) weak red vision (protanomaly), or 3) weak green vision (deuteranomaly). Individuals with two-color vision (dichromats) are those who 1) cannot perceive red (protanopia), 2) cannot perceive green (deuteranopia) or 3) cannot perceive blue (tritanopia). Persons with tritanopia are rare, as are those with no color vision (monochromatomats). Monochromatomats see the environment in shades of light and dark, and some of them experience pain during light stimulation.

Color blindness is usually classed as a mild disability, but there are occasional circumstances where it appears advantageous. Some studies conclude that colorblind people are better at penetrating certain color camouflages. This might indicate an evolutionary advantage to account for the high prevalence of red–green color blindness.

5. The retina is the only tissue in the body in which blood vessels can be observed directly. Examination of the ocular fundi enables the physician to observe the effects of hypertension in a unique vascular bed. The three circulations of the posterior portion of the eye derive from branches of the ophthalmic artery. The retinal circulation is particularly sensitive to local tissue metabolic needs (glucose consumption and oxygen use are 3-fold higher than in any other tis-

sue in the body) and is susceptible to damage from circulatory dysfunction.

**Retinal circulation.** Changes in retinal blood vessels are the most common vascular lesions in the eye due to systemic hypertension. Hypertensive retinopathies have been classified by a number of investigators (*e.g.*, Keith, Wagner, and Baker, 1939, and those of Scheie, 1953), but these classifications are less useful clinically than a careful description of the extent of lesions in the eye. Hypertensive retinopathy may include various combinations of lesions. Some are relatively specific for hypertensive retinopathy, *e.g.*, “copper wiring” of arterioles, “arteriovenous nicking” and related crossing changes, as well as arterial macroaneurysms. Additional “hypertensive” lesions found in other disorders include the “cotton-wool spots” in diabetic retinopathy, systemic lupus erythematosus, retinal vein occlusions, and acquired immune deficiency syndrome. Flame-shaped intraretinal hemorrhages also occur in diabetic retinopathy, profound anemia, the leukemias and other blood dyscrasias. Arterial “silver wiring” may occur in diabetic retinopathy, collagen-vascular diseases, and arterial occlusive diseases.

**Chorioidal circulation.** Hypertensive changes in the chorioidal vessels occur much less frequently than hypertensive changes in the retina. Hypertensive chorioidopathy occurs because the short chorioidal arteries feed at right angles into the chorioidal capillaries, allowing direct transmission of systemic blood pressure to the capillaries. Initial changes may include focal regions of choriocapillary nonperfusion resulting from fibrinoid necrosis of the vessels. These defects are recognized only by the use of specific techniques such as intravenous fluorescein angiography. The retinal pigment epithelium over these nonperfused regions may subsequently develop a yellowish coloration called the Elschnig spot. This eventually becomes a scar with a pigment-ed center and an atrophic surrounding halo.

**Optic nerve circulation.** Hypertensive changes in the optic nerve are relatively uncommon. The principal optic nerve lesion of hypertension is disc edema.

6. Key points for managing ocular trauma include following:

- Take an accurate history.
- Search for foreign bodies under the upper lid.
- Suspect a subtarsal foreign body with persistent pain in an intact eye.
- Irrigate chemical injuries immediately with clean water.
- Suspect a perforating eye injury if the pupil is not round, a cataract develops rapidly or vitreous hemorrhage is present.

7. Several types of specimens may be collected for the microbiological analysis of the eye infections. These include conjunctival scrapings obtained with a swab or sterile spatula for the diagnosis of conjunctivitis, corneal scrapings collected with a sterile spatula for the diagnosis of kerati-

tis, vitreous fluid collected by aspiration for the diagnosis of endophthalmitis, and fluid material collected by aspiration from a tissue biopsy for the diagnosis of periorbital cellulitis.

Direct inoculation of agar culture plates and preparation of smears in the clinic or at the bedside is recommended for the small volumes of specimens collected from corneal scrapings and vitreous fluid. A close working association between the laboratory and ophthalmologist will ensure a supply of appropriate culture media, correct techniques for inoculation media, and rapid transport of plates and smears to the laboratory.

8. Left ventricular hypertrophy (LVH) is the response of the heart to chronic pressure, volume overload, or both. The most common causes of cardiac hypertrophy are hypertension and valvular heart disease. Genetic factors determine the extent of the hypertrophic response to existing stimuli, and several mutations have been identified in kindreds with severe familial forms of LVD. These can occur even in the absence of hypertension.

The diagnosis of LVH can be made in several ways, but it is commonly identified by electrocardiogram (ECG) on the basis of increased voltage and repolarization abnormalities, or by an echocardiogram that calculates left ventricular mass (LVM) from measured LV wall thickness and internal chamber dimensions.

9. The totality of DNA possessed by an individual constitutes his or her genome. Genomics, as distinct from genetics, is the study of the organization and evolutionary history of DNA. The total human genome is approximately three billion bases long; this is the product of two parental genomes of three billion base pairs each (*i.e.*, roughly six billion “bits” of information divided into pairs).

10. There is evidence for a significant genetic component of blood pressure in humans, and several intermediate phenotypes closely associated with hypertension relate directly to specific genes. Intermediate phenotypes are quantifiable biologic traits (such as angiotensinogen levels or salt sensitivity) that, in appropriate combinations, account for a fraction of the overall risk for the development of hypertension.

Numerous linkage analyses using 300 to 500 markers spread over all chromosomes suggest several locations for hypertension genes. Some of the more consistent areas are on chromosome arms 1q, 2p, 2q, 8p, 17q, and 18q. Other less consistent regions may still harbor important genes. Genes involving the renin-angiotensin system have been the ones most systematically studied.

A family history of hypertension is commonly used as a measure of familial aggregation, and it can be a surrogate measure for undefined risk factors shared by the family. Controlling or removing behavioral risk factors confers the

greatest benefit for individuals with the greatest genetic risk. Interactions between genetic variations and environmental factors such as stress, diet, and physical activity also contribute to the development of essential hypertension.

It is well known that hypertensive individuals exhibit a varied response to antihypertensive drugs, likely reflecting a wide variety of factors, including differences in pharmacodynamic and pharmacokinetic traits. Pharmacogenetics, the study of genetic variations that influence responses to pharmacogenetic agents, is an emerging field based upon genetic-environmental interactions.

11. Measurement of blood pressure in children is recommended yearly after the age of three years. The diagnosis of hypertension in children now uses the fifth Korotkoff sound to define diastolic blood pressure. It also depends on height.

The average systolic BP at one day of age is approximately 70 mm Hg in full-term infants, and it increases to approximately 85 mm Hg by one month of age. During the first year of life, BP increases at a greater rate in premature infants than in full-term infants. BP then increases steadily throughout the first two decades of life. Greater weight, greater height, and family history of hypertension are known to be associated with higher levels of BP in children and adolescents.

12. The correct answer is D. Determination of the albumin level can help assess the current extent of starvation in a patient. It is an important index in the treatment of anorexic patients.

13. The correct answer is B. Family therapy, both short-term and long-term, has been shown to improve outcomes in adolescent patients with anorexia nervosa. Many of these family treatments are completed in stages, generally beginning with developing parental control over the eating and gradually turning control over to the adolescent as nutritional status improves. Some cognitive behavioral therapies may be effective, but there is little evidence for the others listed.

14. The correct answer is A.

Comment: This patient's nausea is likely due to gastrointestinal distension and irritation from both constipation and her ovarian cancer; there is possibly a direct effect from the opioid therapy as well. Opioid-induced nausea is primarily mediated by dopamine. In this case, serotonin receptors in the gastrointestinal tract, serosa, and viscera are also involved. Dopamine blockade would likely be helpful for this patient. Metoclopramide, a dopamine D2 receptor antagonist with some peripheral serotonin antagonism, would be the best choice. Prochlorperazine and haloperidol would also be reasonable choices.

Enough time has passed since the patient's most recent chemotherapy that it should not be a major contributor to her

nausea at this time. Importantly, she does not appear to have a bowel obstruction. It is important to rule out obstruction to preclude the need for surgical intervention or nasogastric tube placement. Obstruction should also be ruled out before administering metoclopramide, given the promotility actions of the drug. Anxiety does not seem to be a major component of the patient's condition, and lorazepam alone has poor antiemetic effects.

Toxin-induced nausea, such as medication effects and electrolyte disturbances (*e.g.*, hypercalcemia) are mediated through the chemoreceptor trigger zone (CTZ), within the area postrema in the floor of the fourth ventricle. Serotonin and dopamine are the two most active neurotransmitters in the CTZ. Serotonin antagonists, such as haloperidol, metoclopramide, or prochlorperazine, are most effective for treatment of CTZ-mediated nausea. Promethazine is a weak antagonist of dopamine, and it generally acts by inducing sedation via antihistaminic and anticholinergic pathways. Promethazine is not routinely recommended for nausea, given its limited efficacy and wide range of adverse effects.

Conclusion: Selection of an antiemetic should consider the mechanism of the drug's action and the putative factors that contribute to the nausea.

15. The term presbycusis refers to the hearing loss due to aging. Aging generally affects the cochlea, but it may also affect the central auditory pathway. The deafness of aging is characteristically bilaterally symmetrical and predominantly affects high tones. The basal turn of the cochlea is involved in perception of high tones, while lower turns are appreciated higher up in the cochlear spiral. Because it is nearest the oval window through which vibrations enter the cochlea, the basal turn bears the brunt of 'wear and tear' and hearing for high tones fails first.

In aged individuals, the ear has likely been exposed to one or more other causes of hearing loss. Presbycusis appears to begin earlier in urban than in rural communities.

Pathological changes can affect any of these four sites in the cochlea:

- a. In 'sensory presbycusis' the organ of Corty in the basal turn of the cochlea atrophies, with disappearance of hair cells.
- b. 'Strial presbycusis' exhibits patchy atrophy of the stria vascularis, with cystic changes.
- c. In 'cochlear conductive presbycusis' the basal membrane becomes stiffened and calcified, especially in the basal turn.
- d. 'Neural presbycusis' involves atrophy of the spiral ganglion with severe loss of ganglion cells.

Audiograms reveal that neural presbycusis is associated with severe loss of speech discrimination, and strial presbycusis shows a fairly even hearing loss at all frequencies with good speech discrimination. High tone loss is charac-

teristic of the sensory and cochlear conductive forms.

16. A diet high in cholesterol, saturated fats and fructose (*i.e.*, “fast food”) promotes development of nonalcoholic fatty liver disease (NAFLD), insulin resistance, and metabolic syndrome. The progressive form of NAFLD, nonalcoholic steatohepatitis (NASH), is characterized by inflammation and fat accumulation in the liver, which can lead to cirrhosis and ultimately to loss of liver function.

A newly developed animal model of NASH shows gene expression typical of metabolic syndrome and NASH with progressive fibrosis. It is interesting to note that the observed effects were more pronounced in male mice than in females.

17. When editors or typesetters refer to *style*, they do not mean writing style, but rather editorial style—the rules or guidelines a publisher follows to ensure clear, consistent presentation of the printed word. Editorial style concerns uniform use of punctuation and abbreviations, construction of tables, section of headings, and citation of references, as well as many other elements that are part of every manuscript.

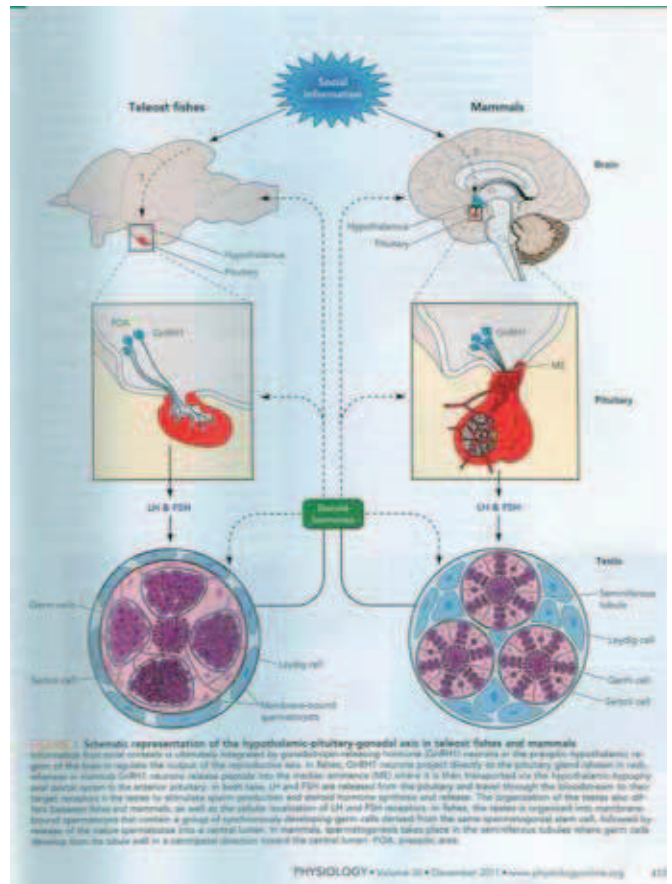
An author writing for a particular publication must follow the style rules established by the publisher to avoid inconsistencies among journal articles or book chapters. For example, without rules of style, three different manuscripts might use *sub-test*, *subtest*, and *Subtest* or *E-mail*, *e-mail* or *email*. Although the meaning of these two words in three variations is the same, and the choice of one style over the other may seem arbitrary (*subtest* and *e-mail* are APA style), such variations in style may distract or confuse the reader.

18. The dynamics of water are very fast, picosecond to tens of picosecond on the time scale. Ultrafast infrared (IR) experiments performed on the hydroxyl (OH) stretch of water can be used to measure the dynamics of water molecules under thermal equilibrium conditions.

Water at an interface behaves differently in a system where the characteristic nanodimension is relatively large (>10 nm) vs. one in which it is small (<4 nm). Water dynamics depend on the nature of the large molecular structures the water is interacting with, but also to an even greater extent on the size of the nanoscopic water system.<sup>1\*</sup>

19. Reproduction in all vertebrates is controlled by the hypothalamic-pituitary-gonadal axis. In many species the social environment influences this axis, and consequently reproductive fitness. Numerous studies in vertebrates demonstrate activation of reproduction by olfactory, auditory, tactile, and visual social signals; these signals can reflect changes in the number, size or axonal densities of gonadotropin-releasing hormone 1 (GnRH1) peptide, either delivered

directly via neuronal projections in fishes or via the hypothalamic-pituitary portal system in tetrapods. The peptide binds to GnRH receptors on these secondary cells to induce synthesis and release of two gonadotropin hormones, LH and FSH, which then target the gonads (testes or ovaries) to stimulate steroid production and gamete development. Social behaviors are defined as interactions among members of the same species that influence immediate or future behaviors, including production, reception, and interpretation of communicative signals in a context-dependent manner.



This Figure is from an article entitled Social Regulation of Gene Expression in the Hypothalamic-Pituitary-Gonadal Axis by Karen P. Maruska and Russell D. Fernald in *Physiology* (2011;26:412-23). Reproduced by permission of The American Physiological Society.

20. Recently introduced medications such as bisphosphonates (alendronate, etidronate, clodronate, pamidronate, risedronate, zoledronate, etc.) are used in the therapy of osteoporosis, Paget's disease and the hypercalcemia of malignancy. These new agents broaden the range of current treatment options. Even though contemporary studies suggest positive effects of bisphosphonates used in everyday practice, there are also risks associated with their use, such as inhibition of osteoclast functions that lead to inhibition of normal bone turnover. This can result in impaired wound

<sup>1\*</sup> We refer to water confined on nanometer length scales as “nanoscopic water.”

healing following trauma (such as dental surgery) or even spontaneous non-healing bone exposure. Because bisphosphonates are preferentially deposited in bone with high turnover rates, the levels of bisphosphonates within jawbones may be elevated selectively. The main dental concern is bisphosphonate-related osteonecrosis of the jaw. Numerous studies indicate a relation between use of bisphosphonates and osteonecrosis after dental extraction. Patients who are taking intravenous bisphosphonates for cancer and must undergo dental extraction have an incidence of osteonecrosis of the jaw of one in 10-15 patients, or 10-15 % of this population.

To date the incidence of jaw osteonecrosis in patients treated with intravenous zoledronic acid and subcutaneous denosumab for osteoporosis is unknown, but it is assumed to be low. Since these substances can be considered as drugs, patients should have their oral health checked before treatment. Their bone turnover will be markedly suppressed post-infusion, and dental extractions must be avoided for at least several months.

However, strontium ranelate or teriparatide pose no risks for osteonecrosis of the jaw. These agents have completely different mechanisms of action than the bisphosphonates. In fact, teriparatide may be a good treatment option for bisphosphonate-related osteonecrosis of the jaw.

21. C-terminal telopeptide (carboxy-terminal collagen crosslinks, also known as CTX) is a serum biomarker for bone turnover. It can be useful in assessing risk and guiding clinical evaluation of the nonsurgical treatment response as well as a guide for timing of surgery to pose the least risk of complications during healing. All patients with bisphosphonate-related osteonecrosis of the jaw were found to have low bone turnover as measured by C-terminal telopeptide at the time of onset. The morning fasting CTX test results cannot predict exactly who will develop bisphosphonate-related osteonecrosis of the jaw. CTX values are useful for stratification of relative risk: less than 100 pg/mL indicates high risk; between 100 pg/mL and 150 pg/mL indicates moderate risk; above 150 pg/mL indicates minimal risk.

22. Xerostomia is subjective complaint of mouth/oral dryness, caused by a reduction in normal salivary secretion due to different causes. Even though there are many treatment modalities available to enhance salivary flow, the therapy often remains unsatisfactory. Unknown etiology and lack of specific therapy make management of this disease very difficult. Low-level laser therapy (LLLT; low-level laser irradiation, photo-bio-modulation) has been used extensively as a non-invasive tool for reduction of xerostomia. LLLT significantly enhances salivary secretion and improves antimicrobial characteristics of secreted saliva (increased levels of secretory immunoglobulin A, sIgA). Furthermore, LLLT improves salivary flow and regeneration of salivary duct epithelial cells. It can be safely and effectively used as an advanced treatment modality for reduction of xerostomia.

23. The causes of color changes in vital teeth are: secondary mineralization after trauma, enamel defects, use of systemic drugs such as fluoride, tetracyclines (tetracycline, oxytetracycline, doxycycline, minocycline)<sup>2\*</sup>, ciprofloxacin, amoxicillin, hemorrhage (after vital extirpation), and exposure to coffee, red wine, tobacco, certain spices, etc. The main causes of the changes in color for nonvital teeth are: pulp necrosis, endodontal drugs and treatment materials such as iodoform, endometasone, and restorative materials, such as amalgam.

24. In patients with acute coronary syndrome (ACS), major bleeding is a significant predictor of worse outcome. Access site complications represent a significant source of bleeding for those patients undergoing revascularization, especially when femoral access is used. Observational data and small randomized trials suggest that radial instead of femoral access for coronary angiography/intervention results in fewer bleeding complications, with preserved and possibly improved efficacy, further translating into mortality benefit in higher-risk patients, such as those with ST-segment elevation myocardial infarction (STEMI).

In the two large randomized trials: Radial Versus Femoral Access for Coronary Intervention (RIVAL) and Radial Versus Femoral Investigation in ST Elevation Acute Coronary Syndrome (RIFLE-STEACS) investigators report a detailed analysis the radial and femoral approaches in patients with STEMI. The RIVAL trial was performed in 32 countries (7,021 patients), and RIFLE-STEACS trial was performed at 4 Italian centers.

In patients with STEMI, radial artery access reduced the primary outcome and mortality. No such benefit was observed in patients with non-ST-segment elevation acute coronary syndrome (NSTEACS). The radial approach may be preferred in STEMI patients, provided adequate operator and center expertise is present

25. Overweight-obesity is defined as a BMI of 27.8 or greater for men and 27.3 or greater for women. The WHO defined preobesity (overweight) as a BMI of 25 or greater and class (grade) 1 obesity as a BMI of 30 or greater, class 2 as a BMI of 35 or greater, and class 3 as a BMI of 40 or greater. Using a sample of more than 2.88 million individuals with more than 270 000 deaths, it was found (Flegal KM, et al. *JAMA* 2012;309:71-82) that all-cause mortality hazard ratios (HRs) relative to normal weight (defined as a BMI of 18.5-<25) for overall obesity (grades 1, 2, and 3 combined; HR, 1.18 [95% CI, 1.12-1.25]). Higher all-cause mortality was not observed in individuals with grade 1 obesity. Mortality was significantly lower among those who were overweight individuals.

Body mass index accounts for about two-thirds of the be-

<sup>2</sup> \*Tetracyclines stain developing teeth, even when taken by the mother during pregnancy. These drugs discolor permanent teeth (yellow-gray-brown), from infancy and childhood to eight years old.

tween-individual variation in total adiposity. Body mass index not account for sex, race, age, and fitness differences in fat mass even at the same body weight. Body mass index is known to be an imperfect predictor of metabolic risk. Some individuals with normal BMI have an overweight-obesity metabolic pattern. Factors such as cardiorespiratory fitness are also independent predictors of total mortality in some groups after controlling for BMI, waist circumference, and percentage of body fat. Newer markers such as those representing systemic inflammation may also extend risk prediction beyond BMI. Establishing BMI is only the first step toward a more comprehensive risk evaluation.

### Literature

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